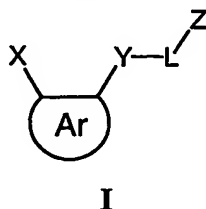


What is claimed is:

1. A compound for modulating kinase activity of Formula I,



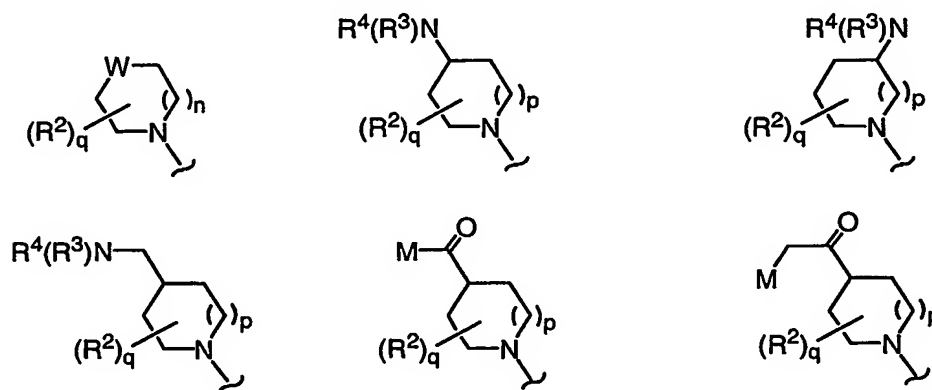
or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is a five- to six-membered aromatic ring system containing between one and three heteroatoms, said five- to six-membered aromatic ring system substituted with -X and -Y-L-Z, in an ortho relationship to each other, and said five- to six-membered aromatic ring system optionally substituted with up to four  $R^1$ ;

each  $R^1$  is independently selected from -H, halogen, -CN, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>3</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, -OC(O)R<sup>3</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl;

optionally two of  $R^1$ , together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of  $R^1$ ;

X is selected from the following six formulae:



wherein,

W is selected from -C(R<sup>2</sup>)(R<sup>2</sup>)-, -N(R<sup>4</sup>)-, -S(O)<sub>0-2</sub>-, and -O-;

n = 1 or 2;

p = 0 or 1;

q is 1 to 3;

M is  $-OR^3$  or  $-N(R^3)R^4$ ;

each  $R^2$  is independently selected from -H, halogen, oxo, -CN,  $-NH_2$ ,  $-NO_2$ ,  $-OR^3$ ,  $-N(R^3)R^3$ ,  $-N(R^3)R^5$ ,  $-S(O)_{0-2}R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^3$ ,  $-N(R^3)SO_2R^3$ ,  $-N(R^3)C(O)R^3$ ,  $-N(R^3)CO_2R^3$ ,  $-N(R^3)C(O)N(R^3)R^3$ ,  $-C(O)R^3$ ,  $-OC(O)R^3$ , optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

two of  $R^2$ , together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each  $R^3$  is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; or

two of  $R^3$ , when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each  $R^4$  is independently selected from  $R^3$ ,  $-SO_2R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^3$ , and  $-C(O)R^3$ ;

Y is selected from  $-CH_2-$ ,  $-O-$ ,  $-S(O)_{0-2}-$ ,  $-N(R^3)-$ , and absent;

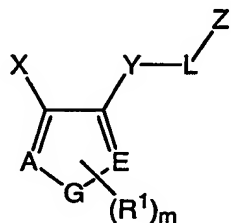
L is selected from  $-(CH_2)_{1-3}-$ ,  $-(CH_2)_{1-3}N(R^3)-$ ,  $-(CH_2)_{1-3}O-$ ,  $-(CH_2)_{1-3}S(O)_{0-2}-$  and absent; each of the aforementioned methylenes optionally substituted;

Z is a five- to seven-membered ring system or  $-R^3$ , said five- to seven-membered ring system optionally substituted with zero to four of  $R^5$ ; and

$R^5$  is selected from -H, halogen, -CN, oxo,  $-NO_2$ ,  $-OR^3$ ,  $-N(R^3)R^4$ ,  $-S(O)_{0-2}R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^3$ ,  $-N(R^3)SO_2R^3$ ,  $-N(R^3)C(O)R^3$ ,  $-N(R^3)CO_2R^3$ ,  $-C(O)R^3$ , optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

optionally two of  $R^5$ , together with the atoms to which they are attached, form a second ring system fused with said five- to seven-membered ring system, said second ring system substituted with zero to four of  $R^5$ .

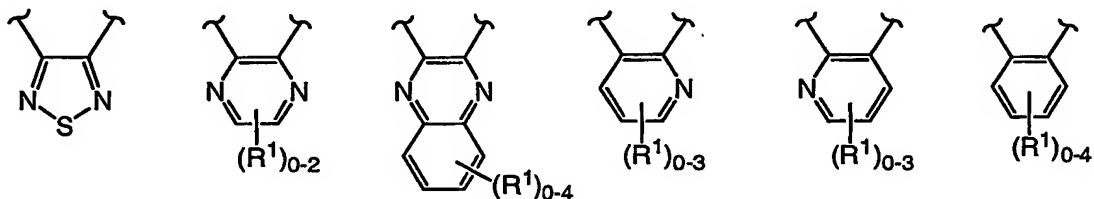
2. The compound according to claim 1, of formula II,



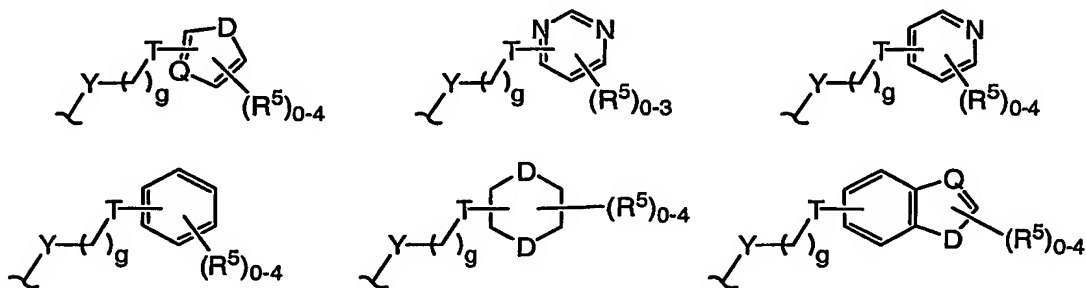
II

wherein, A and E are each independently N or  $-C(R^1)-$ ; and G is selected from  $-S(O)_{0-2}-$ , and  $-C(R^1)=C(R^1)-$ .

3. The compound according to claim 2, wherein Ar is selected from the following formulae.



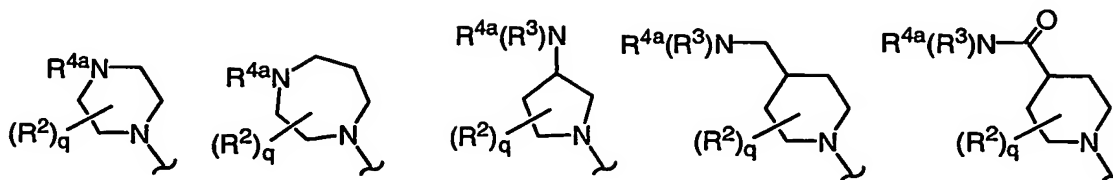
4. The compound according to claim 3, wherein  $-Y-L-Z$  is selected from the following formulae,



wherein g is zero to two; D is selected from  $-C(R^5)(R^5)-$ ,  $-O-$ ,  $-S(O)_{0-2}-$ , and  $-N(R^4)-$ ; Q is  $=N-$  or  $-C(R^5)-$ ; T is selected from absent,  $-N(R^3)-$ ,  $-S-$  and  $-O-$ ; and each methylene between Y and T is optionally substituted; provided that when both Y and T are heteroatoms then g must be two.

5. The compound according to claim 4, wherein Y is  $-O-$  or optionally substituted  $-CH_2-$ .

6. The compound according to claim 5, wherein X is selected from the following formulae.



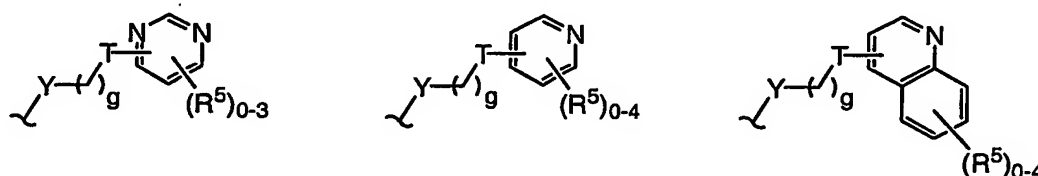
7. The compound according to claim 6, wherein  $R^{4a}$  is selected from  $-\text{SO}_2\text{R}^3$ ,  $-\text{SO}_2\text{N}(\text{R}^3)\text{R}^4$ ,  $-\text{CO}_2\text{R}^3$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^3)\text{R}^4$ , and  $-\text{C}(\text{O})\text{R}^3$ .

8. The compound according to claim 7, wherein each  $\text{R}^2$  is independently selected from  $-\text{H}$  or optionally substituted lower alkyl.

9. The compound according to claim 8, wherein each  $\text{R}^2$  is independently selected from  $-\text{H}$ , haloalkyl,  $-\text{C}_{1-6}\text{alkyl}-\text{N}(\text{R}^3)\text{R}^3$ ,  $-\text{C}_{1-6}\text{alkyl}-\text{OR}^3$ ,  $-\text{C}_{1-6}\text{alkyl}-\text{CO}_2\text{R}^3$ , and  $-\text{C}_{1-6}\text{alkyl}-\text{C}(\text{O})\text{N}(\text{R}^3)\text{R}^3$ .

10. The compound according to claim 9, wherein  $\text{R}^{4a}$  is  $-\text{C}(\text{O})\text{N}(\text{R}^3)\text{R}^3$  or  $-\text{C}(\text{O})\text{R}^3$ .

11. The compound according to claim 10, wherein  $-\text{Y}-\text{L}-\text{Z}$  is selected from the following formulae,

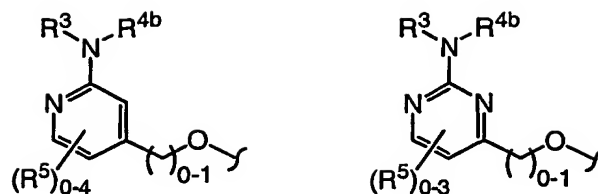


wherein Y, T, and g are as described above.

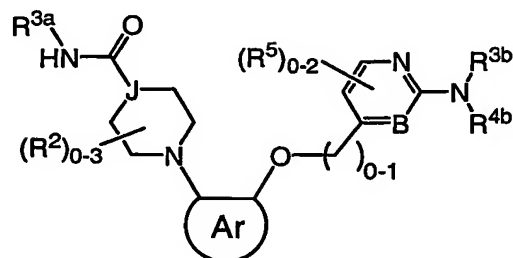
12. The compound according to claim 11, wherein g is one or two.

13. The compound according to claim 12, wherein each  $\text{R}^5$  is independently selected from  $-\text{H}$ , halogen,  $-\text{CN}$ ,  $-\text{NH}_2$ ,  $-\text{NO}_2$ ,  $-\text{OR}^3$ ,  $-\text{N}(\text{R}^3)\text{R}^4$ ,  $-\text{S}(\text{O})_{0-2}\text{R}^3$ ,  $-\text{SO}_2\text{N}(\text{R}^3)\text{R}^3$ ,  $-\text{CO}_2\text{R}^3$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^3)\text{R}^3$ ,  $-\text{N}(\text{R}^3)\text{SO}_2\text{R}^3$ ,  $-\text{N}(\text{R}^3)\text{C}(\text{O})\text{R}^3$ ,  $-\text{N}(\text{R}^3)\text{CO}_2\text{R}^3$ ,  $-\text{C}(\text{O})\text{R}^3$ , and optionally substituted lower alkyl.

14. The compound according to claim 13, wherein  $-\text{Y}-\text{L}-\text{Z}$  is selected from the following formulae.



15. The compound according to claim 14, having formula **III**,



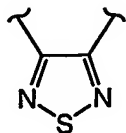
**III**

wherein J is N or CH, and B is =N- or =C(R<sup>5</sup>)-.

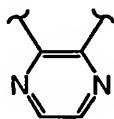
16. The compound according to claim 15, wherein R<sup>3a</sup> is selected from optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl.
17. The compound according to claim 16, wherein R<sup>3a</sup> is selected from optionally substituted aryl and optionally substituted heteroaryl.
18. The compound according to claim 17, wherein R<sup>3a</sup> is optionally substituted phenyl.
19. The compound according to claim 18, wherein said optionally substituted phenyl is substituted with at least one of halogen, -CN, -CF<sub>3</sub>, -NH<sub>2</sub>, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>3</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, optionally substituted lower alkyl, and optionally substituted aryl.
20. The compound according to claim 19, wherein said optionally substituted phenyl group is substituted with at least one trifluoromethyl group.
21. The compound according to claim 20, wherein said optionally substituted phenyl group is substituted with at least two trifluoromethyl groups.
22. The compound according to claim 19, wherein said optionally substituted phenyl group is substituted with at least one lower alkyl group.
23. The compound according to claim 19, wherein R<sup>3b</sup> is -H.

24. The compound according to claim 23, wherein  $R^{4b}$  is selected from  $R^3$ ,  $-H$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^4$ , and  $-C(O)R^3$ .

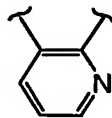
25. The compound according to claim 24, wherein Ar is according to the formula below.



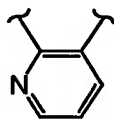
26. The compound according to claim 24, wherein Ar is according to the formula below.



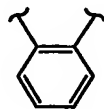
27. The compound according to claim 24, wherein Ar is according to the formula below.



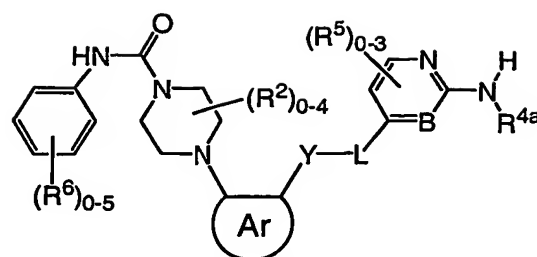
28. The compound according to claim 24, wherein Ar is according to the formula below.



29. The compound according to claim 24, wherein Ar is according to the formula below.



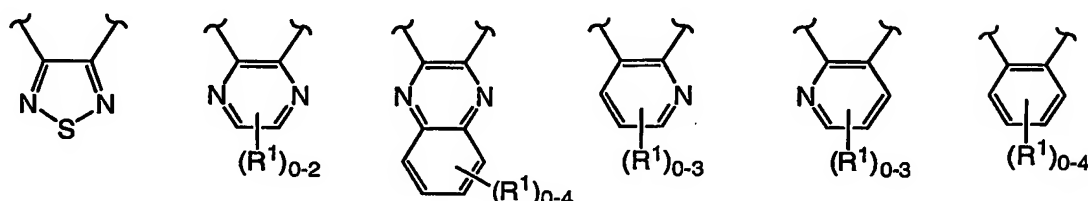
30. A compound for modulating kinase activity of Formula IV,



IV

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is selected from the following formulae:



each  $R^1$  is independently selected from -H, halogen, -CN, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>3</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

optionally two of  $R^1$ , together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of  $R^1$ ;

each  $R^2$  is independently selected from -H, halogen, oxo, -CN, -NH<sub>2</sub>, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)R<sup>5</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)N(R<sup>3</sup>)R<sup>3</sup>, -C(O)R<sup>3</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

two of  $R^2$ , together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each  $R^3$  is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; or

two of  $R^3$ , when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally

substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each  $R^4$  is independently selected from  $R^3$ ,  $-SO_2R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^3$ , and  $-C(O)R^3$ ;

Y is selected from optionally substituted  $-CH_2-$ ,  $-O-$ ,  $-S-$ , and  $-N(R^3)-$ ;

L is selected from optionally substituted  $-CH_2-$ ,  $-O-$ ,  $-S-$ ,  $-N(R^3)-$  and absent;

provided that Y and L are not both heteroatoms;

B is  $=N-$  or  $=C(H)-$ ;

at each instance,  $R^5$  and  $R^6$  are independently selected from  $-H$ , halogen,  $-CN$ ,  $-NO_2$ ,  $-OR^3$ ,  $-N(R^3)R^4$ ,  $-S(O)_{0-2}R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R$ ,  $-N(R^3)SO_2R^3$ ,  $-N(R^3)C(O)R^3$ ,  $-N(R^3)CO_2R^3$ ,  $-C(O)R^3$ , optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

optionally two of  $R^5$ , together with the atoms to which they are attached, form a ring system fused with the ring containing B according to formula IV, said ring system substituted with zero to two additional of  $R^5$ .

31. The compound according to claim 30, wherein Y is  $-O-$  and L is optionally substituted  $-CH_2-$ .

32. The compound according to claim 31, wherein at least one of  $R^6$  is optionally substituted lower alkyl.

33. The compound according to claim 32, wherein said at least one optionally substituted lower alkyl is *meta*- to the piperazine urea function as depicted in formula IV.

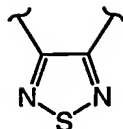
34. The compound according to claim 33, wherein  $R^{4a}$  is selected from  $R^3$ ,  $-H$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^4$ , and  $-C(O)R^3$ .

35. The compound according to claim 34, wherein  $R^{4a}$  is selected from  $-H$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^4$ , and  $-C(O)R^3$ .

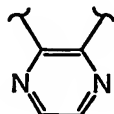
36. The compound according to claim 35, wherein  $-Y-L-$  is  $-OCH_2-$ .

37. The compound according to claim 36, wherein Ar is according to the formula below.

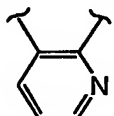




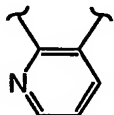
38. The compound according to claim 36, wherein Ar is according to the formula below.



39. The compound according to claim 36, wherein Ar is according to the formula below.



40. The compound according to claim 36, wherein Ar is according to the formula below.



41. The compound according to claim 36, wherein Ar is according to the formula below.



42. The compound according to claim 1, selected from Table 4.

**Table 4**

|   |  |  |
|---|--|--|
| 1 | N-[(1R,2S)-2-phenylcyclopropyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide    |  |
| 2 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |  |

Table 4

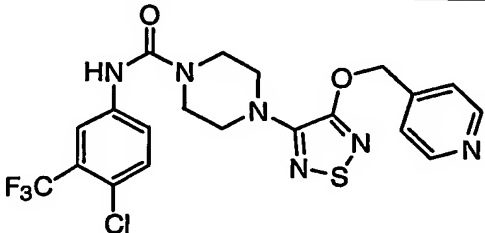
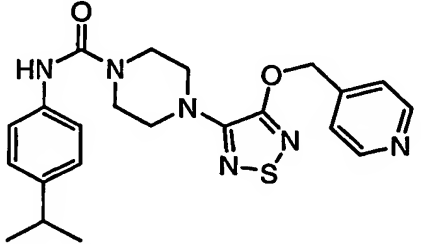
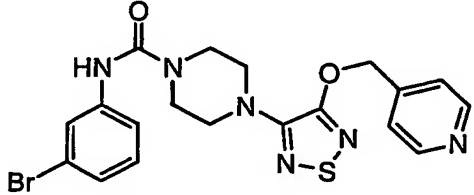
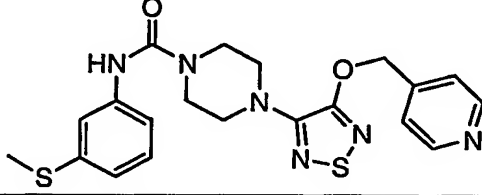
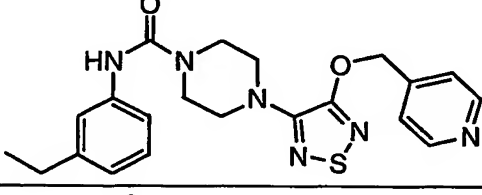
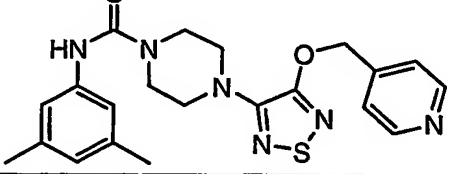
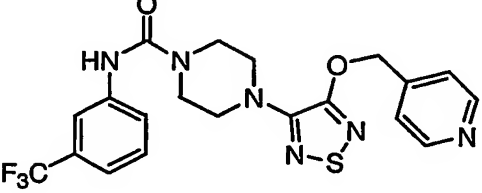
|   |  |  |
|---|--|--|
| 3 | N-[4-chloro-3-(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |    |
| 4 | N-[4-(1-methylethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide            |    |
| 5 | N-(3-bromophenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide                      |    |
| 6 | N-[3-(methylthio)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide               |   |
| 7 | N-(3-ethylphenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide                      |  |
| 8 | N-(3,5-dimethylphenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide                 |  |
| 9 | N-[3-trifluoromethylphenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide            |  |

Table 4

|    |  |  |
|----|--|--|
| 10 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-<br>{[(2-methylquinolin-4-yl)methyl]oxy}-<br>1,2,5-thiadiazol-3-yl)piperazine-1-<br>carboxamide  |  |
| 11 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-<br>{[3-(dimethylamino)phenyl]methyl}oxy]-<br>1,2,5-thiadiazol-3-yl)piperazine-1-<br>carboxamide |  |
| 12 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-<br>(1H-indol-5-yloxy)-1,2,5-thiadiazol-3-<br>yl)piperazine-1-carboxamide                        |  |
| 13 | N-[3,5-bis(trifluoromethyl)phenyl]-4-<br>{4-[(3-thienylmethyl)oxy]-1,2,5-<br>thiadiazol-3-yl}piperazine-1-<br>carboxamide                |  |
| 14 | N-[3,5-bis(trifluoromethyl)phenyl]-4-<br>{4-[(2-morpholin-4-ylethyl)oxy]-1,2,5-<br>thiadiazol-3-yl}piperazine-1-<br>carboxamide          |  |
| 15 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-<br>{[2-(1H-imidazol-1-yl)ethyl]oxy}-1,2,5-<br>thiadiazol-3-yl)piperazine-1-<br>carboxamide      |  |
| 16 | N-[3,5-bis(trifluoromethyl)phenyl]-4-<br>{4-[(1-methylpiperidin-4-yl)oxy]-1,2,5-<br>thiadiazol-3-yl}piperazine-1-<br>carboxamide         |  |
| 17 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-<br>{[4-(methoxy)phenyl]methyl}oxy]-<br>1,2,5-thiadiazol-3-yl)piperazine-1-<br>carboxamide       |  |

Table 4

|    |  |  |
|----|--|--|
| 18 | 4-[4-([3,4-bis(methoxy)phenyl]methyl)oxy]-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide      |  |
| 19 | 4-[4-[(1,3-benzodioxol-5-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide         |  |
| 20 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(furan-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide                   |  |
| 21 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(tetrahydrofuran-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide         |  |
| 22 | N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide        |  |
| 23 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-1,4-diazepane-1-carboxamide             |  |
| 24 | 1-([[(1S,2R,5S)-5-methyl-2-(1-methylethyl)cyclohexyl]oxy}acetyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine |  |
| 25 | 5-phenyl-N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)-1,3-oxazole-4-carboxamide                      |  |

Table 4

|    |  |  |
|----|--|--|
| 26 | 1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-4-[[3-(trifluoromethyl)phenyl]acetyl}piperazine                        |  |
| 27 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(piperidin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide           |  |
| 28 | N-[3,5-bis(trifluoromethyl)phenyl]-N'-[(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperidin-4-yl)methyl]urea      |  |
| 29 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(3-pyridin-3-ylpropyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide           |  |
| 30 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{1,1-dioxido-4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |  |
| 31 | 4-[4-(1-azabicyclo[2.2.2]oct-3-yloxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide      |  |
| 32 | 4-[(4-{4-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl]benzoic acid       |  |

Table 4

|    |  |  |
|----|--|--|
| 33 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(piperidin-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide   |  |
| 34 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-pyrrolidin-1-ylethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |  |
| 35 | 4-{4-[(2-amino-2-methylpropyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide |  |
| 36 | N-[3,5-bis(trifluoromethyl)phenyl]-1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperidine-4-carboxamide     |  |
| 37 | 1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperidine-4-carboxamide          |  |
| 38 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide               |  |
| 39 | 4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide                    |  |
| 40 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-piperidin-4-ylethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide  |  |

Table 4

|    |  |  |
|----|--|--|
| 41 | 2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide |  |
| 42 | 1-phenyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine   |  |
| 43 | 1-[(4-methylphenyl)methyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine                           |  |
| 44 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)amino]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide   |  |
| 45 | 4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]-1,4-diazepane-1-carboxamide      |  |
| 46 | 2-methyl-1-{[2-(methyloxy)phenyl]carbonyl}-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine           |  |
| 47 | N-[5-chloro-2-(methyloxy)phenyl]-N'-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)urea       |  |

Table 4

|    |  |  |
|----|--|--|
| 48 | N-[5-methyl-2-(methyloxy)phenyl]-N'-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)urea                 |  |
| 49 | N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)-N'-[3-(trifluoromethyl)phenyl]urea                    |  |
| 50 | 2-methyl-N-[4-(1-methylethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide             |  |
| 51 | 2-methyl-N-[3-(methylthio)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide                |  |
| 52 | (2R)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |  |
| 53 | (2R)-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide      |  |
| 54 | 1-[4-(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazin-1-yl)phenyl]ethanone                                      |  |



Table 4

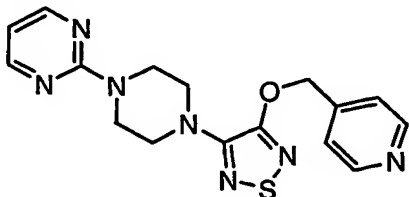
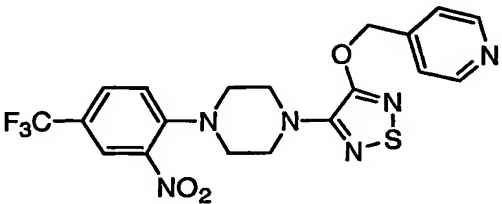
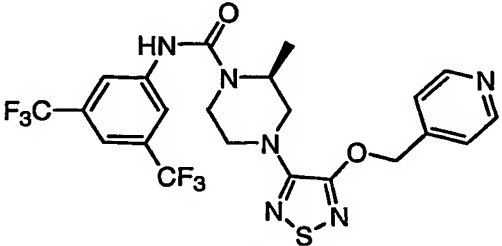
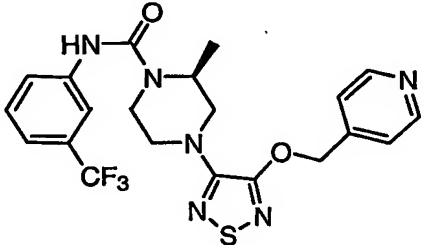
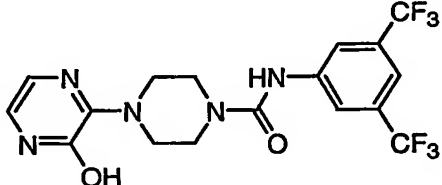
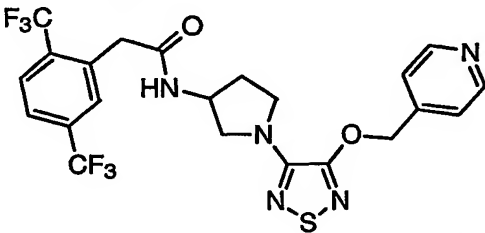
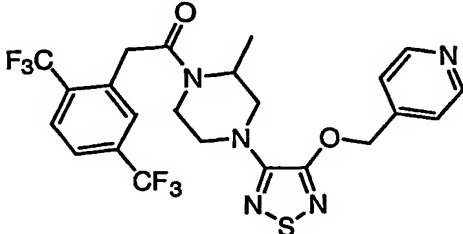
|    |  |  |
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| 55 | 2-(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazin-1-yl)pyrimidine  |    |
| 56 | 1-[2-nitro-4-(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine                          |    |
| 57 | (2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |    |
| 58 | (2S)-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide      |   |
| 59 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-hydroxypyrazin-2-yl)piperazine-1-carboxamide   |  |
| 60 | 2-[2,5-bis(trifluoromethyl)phenyl]-N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)acetamide           |  |
| 61 | 1-{[2,5-bis(trifluoromethyl)phenyl]acetyl}-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine            |  |

Table 4

|    |   |  |
|----|---|--|
| 62 | N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide               |  |
| 63 | 2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide                    |  |
| 64 | N-[3,5-bis(trifluoromethyl)phenyl]-2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide           |  |
| 65 | 2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide                |  |
| 66 | N-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)-N'-[3-(trifluoromethyl)phenyl]urea                             |  |
| 67 | N-[3,5-bis(trifluoromethyl)phenyl]-N'-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)urea                        |  |
| 68 | N-[3,5-bis(trifluoromethyl)phenyl]-2,6-dimethyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |  |

Table 4

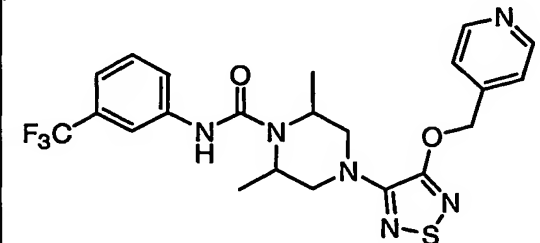
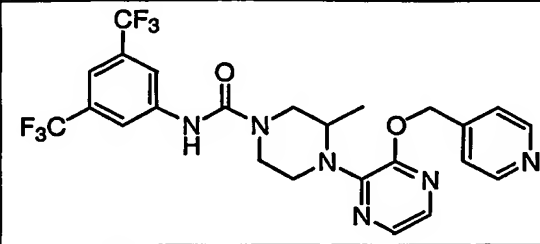
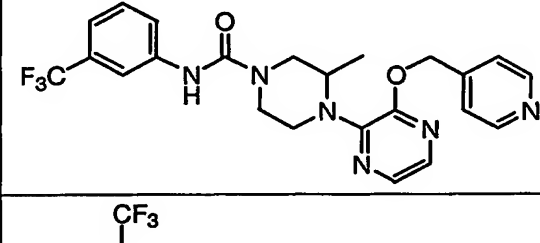
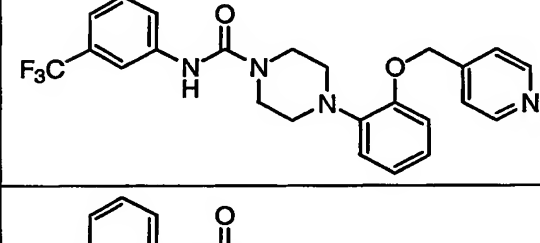
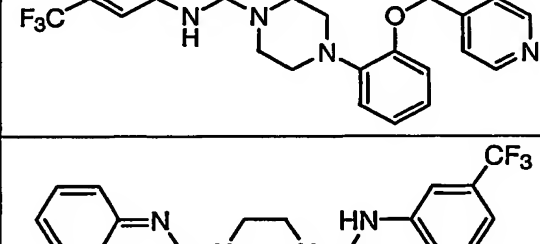
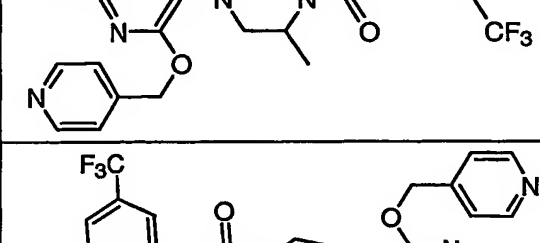
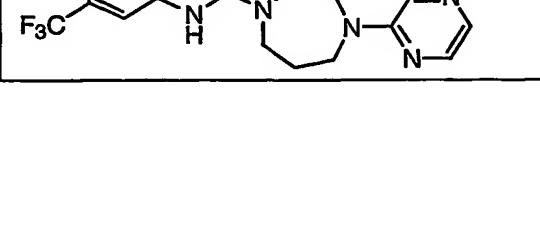
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| 69 | 2,6-dimethyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide |    |
| 70 | N-[3,5-bis(trifluoromethyl)phenyl]-3-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide          |    |
| 71 | 3-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide               |    |
| 72 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{2-[(pyridin-4-ylmethyl)oxy]phenyl}piperazine-1-carboxamide                         |   |
| 73 | 4-{2-[(pyridin-4-ylmethyl)oxy]phenyl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide                              |  |
| 74 | N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}piperazine-1-carboxamide       |  |
| 75 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-1,4-diazepane-1-carboxamide               |  |

Table 4

|    |   |  |
|----|---|--|
| 76 | 2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide             |  |
| 77 | 4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]-1,4-diazepane-1-carboxamide                     |  |
| 78 | N-[3,5-bis(trifluoromethyl)phenyl]-2,5-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide       |  |
| 79 | 2,5-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide            |  |
| 80 | (2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide      |  |
| 81 | (2S)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide           |  |
| 82 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-fluoropyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |  |

Table 4

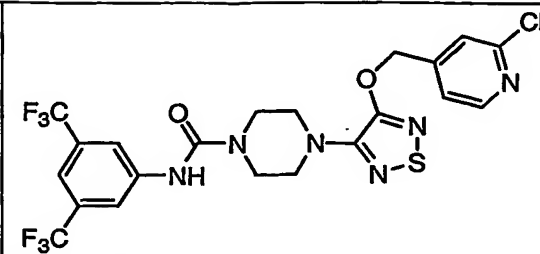
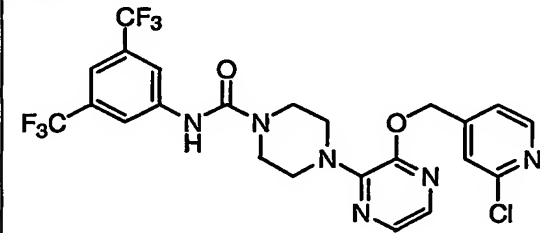
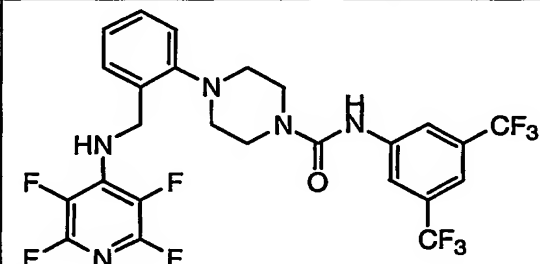
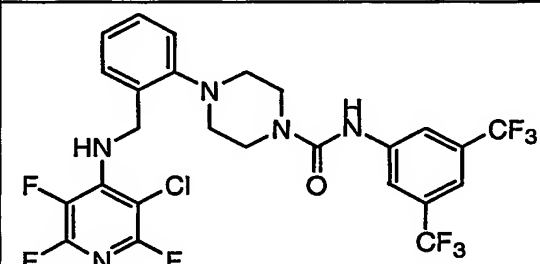
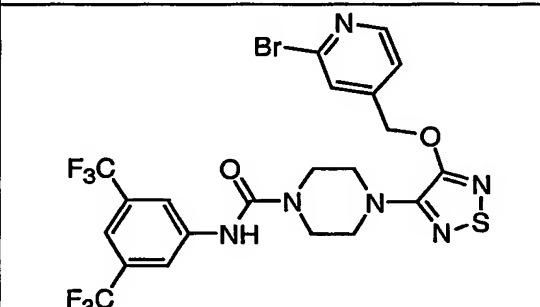
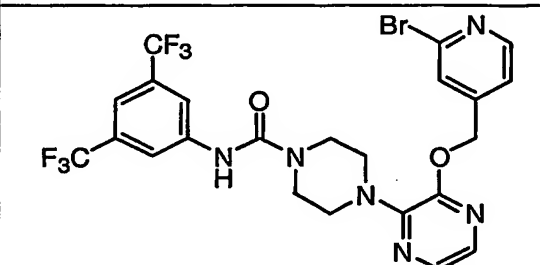
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| 83 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-<br>{[(2-chloropyridin-4-yl)methyl]oxy}-<br>1,2,5-thiadiazol-3-yl)piperazine-1-<br>carboxamide |    |
| 84 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-<br>{[(2-chloropyridin-4-yl)methyl]oxy}pyrazin-2-yl)piperazine-<br>1-carboxamide               |    |
| 85 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(2-<br>{[(2,3,5,6-tetrafluoropyridin-4-yl)amino]methyl}phenyl)piperazine-1-<br>carboxamide        |    |
| 86 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(2-<br>{[(3-chloro-2,5,6-trifluoropyridin-4-yl)amino]methyl}phenyl)piperazine-1-<br>carboxamide   |  |
| 87 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-<br>{[(2-bromopyridin-4-yl)methyl]oxy}-<br>1,2,5-thiadiazol-3-yl)piperazine-1-<br>carboxamide  |  |
| 88 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-<br>{[(2-bromopyridin-4-yl)methyl]oxy}pyrazin-2-yl)piperazine-<br>1-carboxamide                |  |

Table 4

|    |  |  |
|----|--|--|
| 89 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-<br>{[(2-fluoropyridin-4-<br>yl)methyl]oxy}pyrazin-2-yl)piperazine-<br>1-carboxamide   |  |
| 90 | N-[3,5-bis(trifluoromethyl)phenyl]-4-<br>{5,6-dicyano-3-[(pyridin-4-<br>ylmethyl)oxy]pyrazin-2-yl}piperazine-<br>1-carboxamide |  |
| 91 | 4-{5,6-dicyano-3-[(pyridin-4-<br>ylmethyl)oxy]pyrazin-2-yl}-N-[3-<br>(trifluoromethyl)phenyl]piperazine-1-<br>carboxamide      |  |
| 92 | N-(3-ethylphenyl)-4-{3-[(pyridin-4-<br>ylmethyl)oxy]pyrazin-2-yl}piperazine-<br>1-carboxamide                                  |  |
| 93 | N-(3-ethylphenyl)-2-methyl-4-{3-<br>[(pyridin-4-ylmethyl)oxy]pyrazin-2-<br>yl}piperazine-1-carboxamide                         |  |
| 94 | N-(3-ethylphenyl)-2,6-dimethyl-4-{3-<br>[(pyridin-4-ylmethyl)oxy]pyrazin-2-<br>yl}piperazine-1-carboxamide                     |  |

Table 4

|     |   |  |
|-----|---|--|
| 95  | N-(3-ethylphenyl)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}piperazine-1-carboxamide   |  |
| 96  | N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-(2-pyridin-4-ylethyl)pyrazin-2-yl}piperazine-1-carboxamide  |  |
| 97  | N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide  |  |
| 98  | N-[3,5-bis(trifluoromethyl)phenyl]-4-{2-[(pyridin-4-yl)oxy)methyl]phenyl}piperazine-1-carboxamide   |  |
| 99  | 4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide                           |  |
| 100 | 1,1-dimethylethyl {4-[(4-{4-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-yl}carbamate |  |

Table 4

|     |   |  |
|-----|---|--|
| 101 | methyl {4-[(4-[4-({3,5-bis(trifluoromethyl)phenyl}amino)carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl)oxy)methyl}pyridin-2-yl} carbamate |  |
| 102 | 4-{[(4-piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-amine   |  |
| 103 | N-(4-chlorophenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide  |  |
| 104 | 4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide               |  |
| 105 | N-(3-chlorophenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide  |  |
| 106 | 4-{[(4-piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl}-N-propylpyridin-2-amine  |  |



Table 4

|     |  |  |
|-----|--|--|
| 107 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-([2-(propylamino)pyridin-4-yl]methyl)oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide   |  |
| 108 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-([2-(methylamino)pyrimidin-4-yl]methyl)oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide |  |
| 109 | N-methyl-4-[[4-(piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy]methyl]pyridin-2-amine   |  |
| 110 | N-ethyl-4-[[4-(piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy]methyl]pyridin-2-amine  |  |
| 111 | N-butyl-4-[[4-(piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy]methyl]pyridin-2-amine  |  |
| 112 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-([2-(methylamino)pyridin-4-yl]methyl)oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide   |  |

Table 4

|     |   |  |
|-----|---|--|
| 113 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-<br>([2-(ethylamino)pyridin-4-<br>yl]methyl)oxy]-1,2,5-thiadiazol-3-<br>yl]piperazine-1-carboxamide             |  |
| 114 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-<br>([2-(butylamino)pyridin-4-<br>yl]methyl)oxy]-1,2,5-thiadiazol-3-<br>yl]piperazine-1-carboxamide             |  |
| 115 | N-[3,5-bis(trifluoromethyl)phenyl]-4-<br>{4-[(2-[(phenylmethyl)amino]pyridin-<br>4-yl)methyl]oxy}-1,2,5-thiadiazol-3-<br>yl}piperazine-1-carboxamide    |  |
| 116 | N-[3,5-bis(trifluoromethyl)phenyl]-4-<br>{4-[(2-[(1-methylethyl)amino]pyrimidin-4-<br>yl)methyl]oxy}-1,2,5-thiadiazol-3-<br>yl}piperazine-1-carboxamide |  |
| 117 | N-[3,5-bis(trifluoromethyl)phenyl]-4-<br>{4-[(2-[(phenylmethyl)amino]pyrimidin-4-<br>yl)methyl]oxy}-1,2,5-thiadiazol-3-<br>yl}piperazine-1-carboxamide  |  |

Table 4

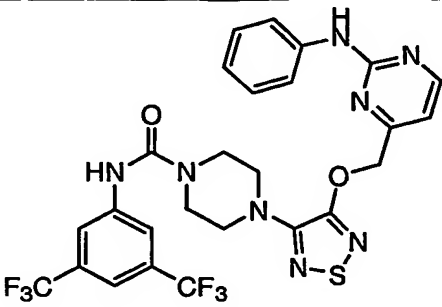
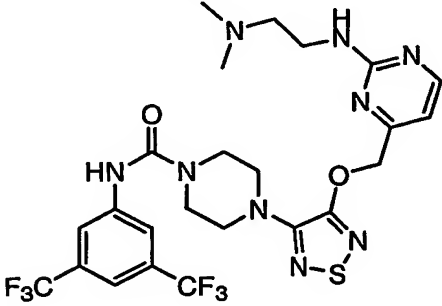
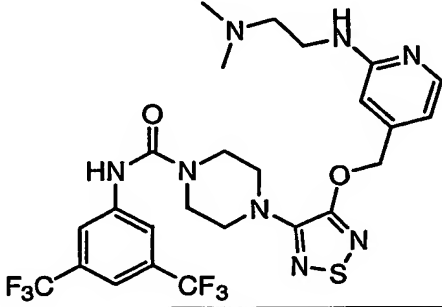
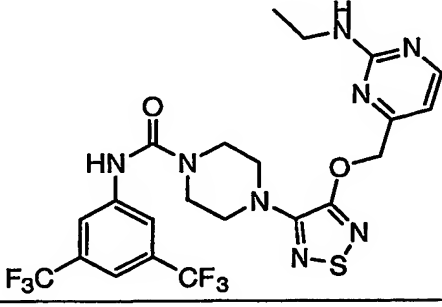
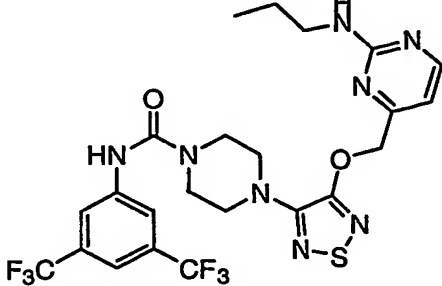
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|-----|--|--|
| 118 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-<br>( {[2-(phenylamino)pyrimidin-4-<br>yl]methyl}oxy)-1,2,5-thiadiazol-3-<br>yl]piperazine-1-carboxamide                           |    |
| 119 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-<br>{ [(2-{ [2-<br>(dimethylamino)ethyl]amino } pyrimidin-<br>4-yl)methyl]oxy }-1,2,5-thiadiazol-3-<br>yl)piperazine-1-carboxamide |    |
| 120 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-<br>{ [(2-{ [2-<br>(dimethylamino)ethyl]amino } pyridin-4-<br>yl)methyl]oxy }-1,2,5-thiadiazol-3-<br>yl)piperazine-1-carboxamide   |   |
| 121 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-<br>( {[2-(ethylamino)pyrimidin-4-<br>yl]methyl}oxy)-1,2,5-thiadiazol-3-<br>yl]piperazine-1-carboxamide                            |  |
| 122 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-<br>( {[2-(propylamino)pyrimidin-4-<br>yl]methyl}oxy)-1,2,5-thiadiazol-3-<br>yl]piperazine-1-carboxamide                           |  |

Table 4

|     |  |  |
|-----|--|--|
| 123 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-([2-(cyclopropylamino)pyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide      |  |
| 124 | 4-[4-([2-(acetylamino)pyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide           |  |
| 125 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-(phenylcarbonyl)amino)pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide    |  |
| 126 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-(phenylcarbonyl)amino)pyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide  |  |
| 127 | 4-{4-[(2-bis(phenylcarbonyl)amino)pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide |  |

Table 4

|     |   |  |
|-----|---|--|
| 128 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-([2-(cyclopentylamino)pyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide                                   |  |
| 129 | 4-[4-([2-(acetylamino)pyridin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide  |  |
| 130 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[[2-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl]amino]pyridin-4-yl}methyl]oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide |  |
| 131 | methyl {4-[[4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl]piperazin-1-yl]-1,2,5-thiadiazol-3-yl]oxy)methyl]pyrimidin-2-yl} carbamate                               |  |
| 132 | 4-(4-[[2-(aminopyridin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide  |  |

Table 4

|     |  |  |
|-----|--|--|
| 133 | methyl [4-({[4-(4-{{(3-ethylphenyl)amino}carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyridin-2-yl]carbamate                |  |
| 134 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-{{[(2-cyanopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide             |  |
| 135 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl})-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide                      |  |
| 136 | 4-[(4-{{[4-(4-{{[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl]pyrimidine-2-carboxamide |  |
| 137 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-{{[2-(butyloxy)pyrimidin-4-yl]methyl}oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide         |  |

Table 4

|     |  |  |
|-----|--|--|
| 138 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyrimidin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide   |  |
| 139 | 4-[[[4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl]piperazin-1-yl]-1,2,5-thiadiazol-3-yl]oxy)methyl]pyridine-2-carboxylic acid                      |  |
| 140 | 2-pyrrolidin-1-ylethyl {4-[[[4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl]piperazin-1-yl]-1,2,5-thiadiazol-3-yl]oxy)methyl]pyridin-2-yl} carbamate |  |
| 141 | 2-morpholin-4-ylethyl {4-[[[4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl]piperazin-1-yl]-1,2,5-thiadiazol-3-yl]oxy)methyl]pyridin-2-yl} carbamate  |  |
| 142 | 4-(3-[[[(2-aminopyrimidin-4-yl)methyl]oxy]pyridin-2-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide   |  |

Table 4

|     |  |  |
|-----|--|--|
| 143 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-<br>{[(2-{{[(1-methylpiperidin-3-<br>yl)carbonyl]amino}pyridin-4-<br>yl)methyl]oxy}-1,2,5-thiadiazol-3-<br>yl)piperazine-1-carboxamide   |  |
| 144 | 4-(3-{{[(2-aminopyrimidin-4-<br>yl)methyl]oxy}pyridin-2-yl)-N-(3-<br>ethylphenyl)piperazine-1-carboxamide  |  |
| 145 | 2-(4-methylpiperazin-1-yl)ethyl {4-[[4-<br>{[(3,5-<br>bis(trifluoromethyl)phenyl]amino}carbo<br>nyl)piperazin-1-yl]-1,2,5-thiadiazol-3-<br>yl]oxy)methyl]pyridin-2-yl} carbamate |  |
| 146 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-<br>{[(2-{{[(1-ethylpiperidin-4-<br>yl)carbonyl]amino}pyridin-4-<br>yl)methyl]oxy}-1,2,5-thiadiazol-3-<br>yl)piperazine-1-carboxamide    |  |
| 147 | 4-(4-{{[(2-aminopyridin-4-<br>yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-<br>N-{3-<br>[(trifluoromethyl)thio]phenyl}piperazin<br>e-1-carboxamide                                      |  |



Table 4

|     |   |  |
|-----|---|--|
| 148 | 4-({[4-(4-{[3,5-bis(trifluoromethyl)phenyl]sulfonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyridin-2-amine                              |  |
| 149 | 4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-naphthalen-1-ylpiperazine-1-carboxamide  |  |
| 150 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(N,N-dimethylglycyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide    |  |
| 151 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(morpholin-4-yl)acetyl]amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |  |
| 152 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(piperidin-1-yl)acetyl]amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide |  |

Table 4

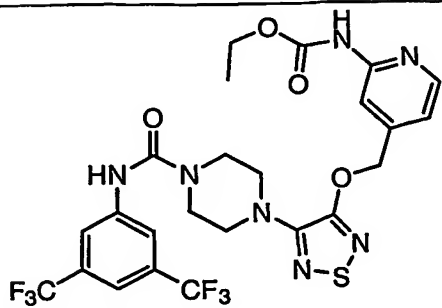
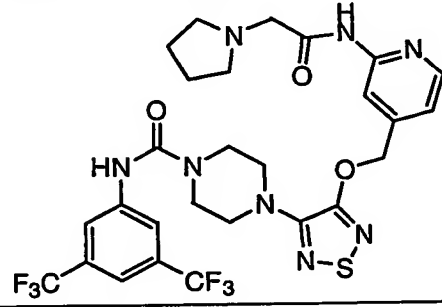
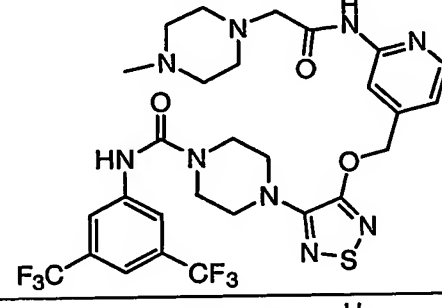
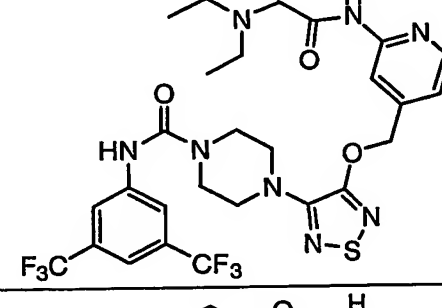
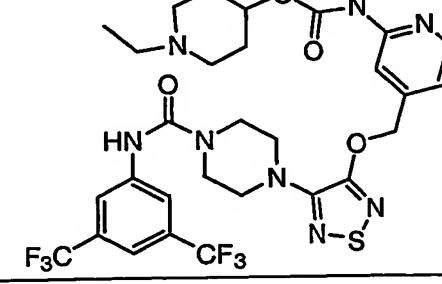
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| 153 | ethyl {4-[(4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-yl} carbamate                   |    |
| 154 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(pyrrolidin-1-yl)acetyl]amino)pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide         |    |
| 155 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-{[(2-[(4-methylpiperazin-1-yl)acetyl]amino)pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide |   |
| 156 | N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(N,N-diethylglycyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide              |  |
| 157 | 1-ethylpiperidin-4-yl {4-[(4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-yl} carbamate   |  |

Table 4

|     |   |  |
|-----|---|--|
| 158 | 4-(4-[(2-aminopyrimidin-4-yl)methoxy]-1,2,5-thiadiazol-3-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide  |  |
| 159 | N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-([2-(2-oxo-1,3-oxazolidin-3-yl)pyridin-4-yl)methoxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide                 |  |
| 160 | 2-(diethylamino)ethyl {4-[(4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl]piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-yl} carbamate    |  |
| 161 | methyl [4-([2-(4-[(3-ethylphenyl)amino]carbonyl]piperazin-1-yl)pyridin-3-yl]oxy)methyl]pyridin-2-yl} carbamate  |  |
| 162 | 2-pyrrolidin-1-ylethyl {4-[(4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl]piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl}pyrimidin-2-yl} carbamate |  |

Table 4

|     |   |  |
|-----|---|--|
| 163 | 2-piperidin-1-ylethyl {4-[(4-{[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl} carbamate |  |
| 164 | methyl [4-({[2-(4-{[(3-bromophenyl)amino]carbonyl}piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]carbamate   |  |
| 165 | methyl {4-[(2-[4-({[3-(methyloxy)phenyl]amino}carbonyl)piperazin-1-yl]pyridin-3-yl]oxy)methyl]pyridin-2-yl} carbamate                                   |  |
| 166 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(methyloxy)phenyl]piperazine-1-carboxamide  |  |
| 167 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide  |  |
| 168 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-[(trifluoromethoxy)phenyl]piperazine-1-carboxamide  |  |
| 169 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                                   |  |

Table 4

|     |   |  |
|-----|---|--|
| 170 | N-(3-ethylphenyl)-4-[3-({[2-({[(3-ethylphenyl)amino]carbonyl}amino)pyridin-4-yl]methyl}oxy)pyridin-2-yl]piperazine-1-carboxamide                  |  |
| 171 | N-(3-ethylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide                  |  |
| 172 | N-(3-ethylphenyl)-4-(4-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide        |  |
| 173 | N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide |  |
| 174 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide                                      |  |

Table 4

|     |  |  |
|-----|--|--|
| 175 | 4-[3-([2-(acetylamino)pyridin-4-yl)methyl]oxy)pyridin-2-yl]-N-(3-ethylphenyl)piperazine-1-carboxamide                |  |
| 176 | 4-(3-([2-(aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide            |  |
| 177 | 2-[4-(3-([2-(aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)piperazin-1-yl]-N-[3,5-bis(trifluoromethyl)phenyl]acetamide |  |
| 178 | 4-(3-([2-(aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)-N-phenylpiperazine-1-carboxamide                              |  |
| 179 | 4-(3-([2-(aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide            |  |
| 180 | 4-(3-([2-(aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide            |  |
| 181 | 4-(3-([2-(aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide             |  |

Table 4

|     |  |  |
|-----|--|--|
| 182 | 2-(4-methylpiperazin-1-yl)ethyl [4-({[2-(4-{[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]carbamate |  |
| 183 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-chlorophenyl)piperazine-1-carboxamide                                       |  |
| 184 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-bromophenyl)piperazine-1-carboxamide  |  |
| 185 | N-[4-({[2-(4-acetyl)piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]-2-(4-methylpiperazin-1-yl)acetamide                             |  |
| 186 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide                                       |  |
| 187 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(4-fluorophenyl)piperazine-1-carboxamide                                       |  |
| 188 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-fluorophenyl)piperazine-1-carboxamide                                       |  |

Table 4

|     |   |  |
|-----|---|--|
| 189 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide                    |  |
| 190 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide                |  |
| 191 | N-methyl-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide |  |
| 192 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide   |  |
| 193 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide              |  |
| 194 | 4-(3-{[(2-amino-5-bromopyrimidin-4-yl)methyl]oxy}-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide        |  |
| 195 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-fluoro-3-(trifluoromethyl)phenyl]piperazine-1-carboxamide   |  |



Table 4

|     |   |  |
|-----|---|--|
| 196 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                     |  |
| 197 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide                                     |  |
| 198 | N-(3-chloro-5-ethylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide |  |
| 199 | N-(5-ethyl-2-fluorophenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide |  |
| 200 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                      |  |
| 201 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide  |  |

Table 4

|     |  |  |
|-----|--|--|
| 202 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide                              |  |
| 203 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide                              |  |
| 204 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-methylpiperazine-1-carboxamide  |  |
| 205 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-ethylpiperazine-1-carboxamide   |  |
| 206 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-cyclohexylpiperazine-1-carboxamide  |  |
| 207 | 4-({[2-(4-acetylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin-2-amine   |  |
| 208 | 4-({[2-(4-propanoylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin-2-amine  |  |
| 209 | N-(3-cyclopropylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide |  |

Table 4

|     |   |  |
|-----|---|--|
| 210 | 4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-(3-cyclopropylphenyl)piperazine-1-carboxamide  |  |
| 211 | N-[2-fluoro-5-(trifluoromethyl)phenyl]-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide |  |
| 212 | N-[3-fluoro-5-(trifluoromethyl)phenyl]-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide |  |
| 213 | N-(3,5-dichlorophenyl)-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide                 |  |
| 214 | 4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide          |  |
| 215 | 4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide  |  |

Table 4

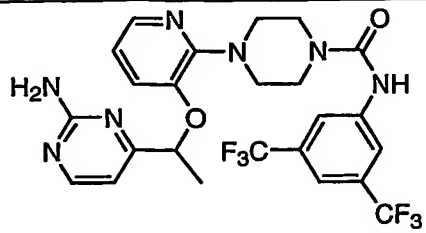
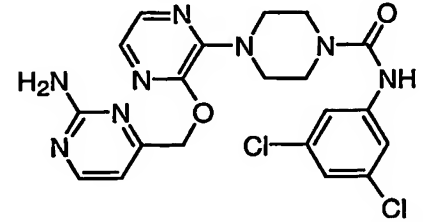
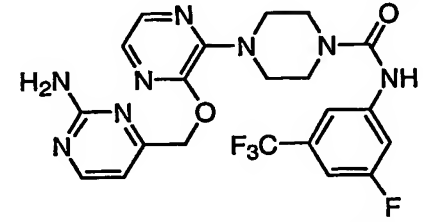
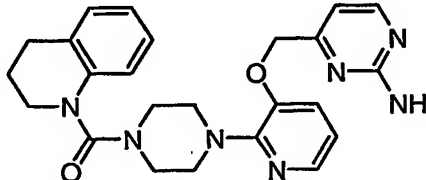
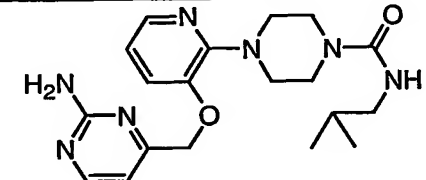
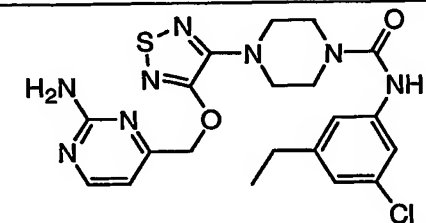
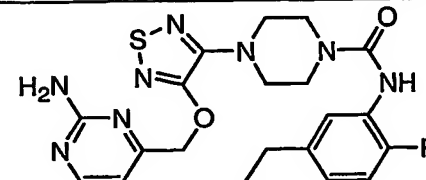
|     |  |  |
|-----|--|--|
| 216 | 4-(3-{{[1-(2-aminopyrimidin-4-yl)ethyl]oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide    |    |
| 217 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide                 |    |
| 218 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide |    |
| 219 | 4-[[{2-[4-(3,4-dihydroquinolin-1(2H)-ylcarbonyl)piperazin-1-yl]pyridin-3-yl]oxy)methyl]pyrimidin-2-amine               |   |
| 220 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-methylpropyl)piperazine-1-carboxamide                     |  |
| 221 | 4-(4-{{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide   |  |
| 222 | 4-(4-{{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide   |  |

Table 4

|     |  |  |
|-----|--|--|
| 223 | 4-(4-[(2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide                     |  |
| 224 | 4-(3-[(2-aminopyrimidin-4-yl)methyl]oxy)pyrazin-2-yl)-N-phenylpiperazine-1-carboxamide   |  |
| 225 | 4-(3-[(2-aminopyrimidin-4-yl)methyl]oxy)pyrazin-2-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide               |  |
| 226 | N-(3,5-diethylphenyl)-4-(3-[(2-[(4-methylpiperazin-1-yl)acetyl]amino)pyridin-4-yl]oxy)methyl]pyridin-2-yl)piperazine-1-carboxamide |  |
| 227 | 4-(3-[(2-aminopyrimidin-4-yl)methyl]oxy)-6-methylpyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide                           |  |
| 228 | 4-(3-[(2-aminopyrimidin-4-yl)methyl]oxy)-6-methylpyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide          |  |
| 229 | 4-(3-[(2-aminopyrimidin-4-yl)methyl]oxy)pyrazin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide                        |  |

Table 4

|     |   |  |
|-----|---|--|
| 230 | 4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-phenylpiperazine-1-carboxamide   |  |
| 231 | 4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide                            |  |
| 232 | 4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                   |  |
| 233 | N-[3-chloro-5-(trifluoromethyl)phenyl]-4-(3-{{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide |  |
| 234 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                            |  |
| 235 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                            |  |
| 236 | 4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide   |  |

Table 4

|     |   |  |
|-----|---|--|
| 237 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide   |  |
| 238 | 4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide  |  |
| 239 | 4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                           |  |
| 240 | 4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                           |  |
| 241 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide   |  |
| 242 | 4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide  |  |
| 243 | N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]-4-(3-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide |  |

Table 4

|     |  |  |
|-----|--|--|
| 244 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide               |  |
| 245 | 4-(3-{[1-(2-aminopyrimidin-4-yl)ethyl]oxy}pyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide  |  |
| 246 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide                       |  |
| 247 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-ethyl-5-fluorophenyl)piperazine-1-carboxamide                                |  |
| 248 | 4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide |  |
| 249 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide           |  |
| 250 | 4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]-N-methylpiperazine-1-carboxamide               |  |



Table 4

|     |  |  |
|-----|--|--|
| 251 | 4-(3-[[2-aminopyrimidin-4-yl)methyl]oxy]pyrazin-2-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide                  |  |
| 252 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide         |  |
| 253 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-(3-chloro-4-fluorophenyl)piperazine-1-carboxamide        |  |
| 254 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-[2,5-bis(methyloxy)phenyl]piperazine-1-carboxamide       |  |
| 255 | 4-(2-[[2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide                 |  |
| 256 | 4-(2-[[2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-ethylphenyl)piperazine-1-carboxamide                                  |  |
| 257 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide        |  |
| 258 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-[3-[(trifluoromethyl)oxy]phenyl]piperazine-1-carboxamide |  |

Table 4

|     |  |  |
|-----|--|--|
| 259 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-[3-(methyloxy)phenyl]piperazine-1-carboxamide                |  |
| 260 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide  |  |
| 261 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide            |  |
| 262 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-[2-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide |  |
| 263 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide                     |  |
| 264 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-[2-(ethyloxy)phenyl]piperazine-1-carboxamide                 |  |
| 265 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-(3,4-difluorophenyl)piperazine-1-carboxamide                 |  |
| 266 | 4-(4-[[2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-[3-(methylthio)phenyl]piperazine-1-carboxamide               |  |

Table 4

|     |  |  |
|-----|--|--|
| 267 | N-(3-acetylphenyl)-4-(4-[(2-aminopyrimidin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide                         |  |
| 268 | 4-(2-[(2-aminopyrimidin-4-yl)methyl]oxy)phenyl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                     |  |
| 269 | 4-(2-[(2-aminopyrimidin-4-yl)methyl]oxy)phenyl)-N-(3-fluorophenyl)piperazine-1-carboxamide   |  |
| 270 | 4-(2-[(2-aminopyrimidin-4-yl)methyl]oxy)phenyl)-N-phenylpiperazine-1-carboxamide   |  |
| 271 | 4-(2-[(2-aminopyrimidin-4-yl)methyl]oxy)phenyl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide                                     |  |
| 272 | 4-(2-[(2-aminopyrimidin-4-yl)methyl]oxy)phenyl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                     |  |
| 273 | 4-[4-([6,7-bis(methoxy)quinolin-4-yl]methyl]oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide |  |

Table 4

|     |   |  |
|-----|---|--|
| 274 | 4-([4-(4-([3,5-bis(trifluoromethyl)phenyl]acetyl)piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl]pyrimidin-2-amine               |  |
| 275 | 5-([(2-aminopyrimidin-4-yl)methyl]oxy)-6-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl]piperazin-1-yl]pyrazine-2-carboxamide |  |
| 276 | 4-(4-([6,7-bis(methyloxy)quinolin-4-yl]oxy)-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide     |  |
| 277 | 4-(2-([(2-aminopyrimidin-4-yl)methyl]oxy)phenyl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide                    |  |
| 278 | 4-(2-([(2-aminopyrimidin-4-yl)methyl]oxy)phenyl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide                               |  |
| 279 | 4-(2-([(2-aminopyrimidin-4-yl)methyl]oxy)phenyl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide                                    |  |

Table 4

|     |  |  |
|-----|--|--|
| 280 | 4-[(4-[4-(naphthalen-2-ylacetyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl)oxy)methyl]pyrimidin-2-amine   |  |
| 281 | 4-(2-[[[(2-aminopyrimidin-4-yl)methyl]oxy]phenyl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide |  |

43. A pharmaceutical composition comprising the compound according to any one of claims 1 - 42 and a pharmaceutically acceptable carrier.

44. A metabolite of the compound or the pharmaceutical composition according to any one of claims 1 - 43.

45. A method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of a composition comprising at least one of the compound according to any of claims 1 - 42 and the pharmaceutical composition according to claim 43.

46. The method according to claim 45, wherein the kinase is Tie-2.

47. The method according to claim 46, wherein modulating the *in vivo* activity of Tie-2 comprises inhibition of Tie-2.

48. A method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of a composition comprising at least one of the compound according to any of claims 1 - 42 and the pharmaceutical composition according to claim 43.

49. A method of screening for modulator of a Tie-2 kinase, the method comprising combining either a composition comprising at least one of the compound according to any of claims 1 - 42 and the pharmaceutical composition according to claim 43, and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.

50. A method of inhibiting proliferative activity in a cell, the method comprising administering to said cell an effective amount of at least one of the compound according to any of claims 1 - 42 and the pharmaceutical composition according to claim 43.